

**Wnt proteins promote bone regeneration.**

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**Funding Grants:** Enhancing healing via Wnt-protein mediated activation of endogenous stem cells

**Public Summary:**

**Scientific Abstract:**

The Wnt signaling pathway plays a central role in bone development and homeostasis. In most cases, Wnt ligands promote bone growth, which has led to speculation that Wnt factors could be used to stimulate bone healing. We gained insights into the mechanism by which Wnt signaling regulates adult bone repair through the use of the mouse strain Axin2(LacZ/LacZ) in which the cellular response to Wnt is increased. We found that bone healing after injury is accelerated in Axin2(LacZ/LacZ) mice, a consequence of more robust proliferation and earlier differentiation of skeletal stem and progenitor cells. In parallel, we devised a biochemical strategy to increase the duration and strength of Wnt signaling at the sites of skeletal injury. Purified Wnt3a was packaged in liposomal vesicles and delivered to skeletal defects, where it stimulated the proliferation of skeletal progenitor cells and accelerated their differentiation into osteoblasts, cells responsible for bone growth. The end result was faster bone regeneration. Because Wnt signaling is conserved in mammalian tissue repair, this protein-based approach may have widespread applications in regenerative medicine.

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